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MARIJUANA USE, ADOLESCENT PREGNANCY, AND ALTERATION IN NEWBORN BEHAVIOR: HOW COMPLEX CAN IT GET?

The study by Barros et al¹ in this issue of *The Journal* raises multiple issues for practice and research, namely marijuana use by adolescents, adolescent pregnancy, and newborn behavioral outcomes. Marijuana, the most-consumed illegal drug in the world, is derived from *Cannabis sativa* (Latin for "planted hemp"), the earliest non-food bearing plant cultivated by humans.² Evidence of cannabis use for medicinal purposes dates back thousands of years. Of the >400 chemicals found in the cannabis plant, only 61 are unique to marijuana. The primary psychoactive constituents of cannabis are Δ^8 -tetrahydrocannabinol (Δ^8 -THC) and Δ^9 -tetrahydrocannabinol (THC).³ THC is the most studied chemical, more prevalent in marijuana, and more potent in vivo than Δ^8 -THC. Marijuana, the dried cannabis leaf material, contains 2% to 4% THC. THC binds to receptors and mimics the action of endogenous cannabinoids.² Cannabinoids produce their pharmacologic effects through a specific family of receptors, 2 of which, CB₁ and CB₂, have been widely studied.⁴

Effects from perinatal administration of marijuana differ according to brain areas and sex. In experimental animals, administration of marijuana during gestation was associated with alteration of the normal development of nigrostriatal, mesolimbic, and tuberoinfundibular dopaminergic neurons.⁵ In rat offspring, learning deficit and decreased emotional reactivity after prenatal marijuana administration have been attributed to decreased number of cortical neurons, deficit in glutaminergic neurotransmission, and reduced N-methyl-D-aspartate (NMDA) receptor activity.⁶ In the human fetus at mid-gestation, reduced D2 messenger RNA expression levels in the amygdala basal nucleus have been noted; these findings correlated with the amount of maternal marijuana intake during pregnancy.⁷ THC readily crosses the placenta early in pregnancy. Animal studies have shown that the fetal serum concentration of THC is about 10% that of maternal levels.

However, repeated use results in increasing concentration in maternal serum and, likewise, increased fetal levels.⁸

The adverse effects of marijuana exposure on the fetus are difficult to scientifically evaluate for a variety of reasons. Wide variation exists in the concentration of the active ingredients found in the product available on the street (anywhere from trace amounts to 20% THC). Comorbidities are also associated with marijuana and other drug use. Adolescents may have poor nutrition, may also use other substances (licit and illicit), or may have poor mental health (have psychiatric disorders such as attention-deficit/hyperactivity disorder, learning disorder, bipolar disorder, or depression).⁹ The amount and duration of drug use are also difficult to determine. Self-reported information may not be reliable because of recall bias or because the adolescent denies use for multiple reasons, including fear of legal scrutiny. Detection of metabolites in meconium will establish fetal drug exposure, but the procedure is highly sensitive only from mid-gestation. Metabolites in biological specimens are indicators of exposure, but concentrations do not accurately reflect quantity of use or when in gestation use occurred. Barros et al¹ analyzed maternal hair to determine neonatal marijuana exposure. However, because of a possibility of environmental contamination of maternal hair, the observed incidence of exposure may be overestimated.

Prenatal marijuana use has effects on fetal physical growth and neurobehavior. In a

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meta-analysis,¹⁰ prenatal marijuana use <1 times per week did not result in a significant decrease in birth weight, but use >4 times per week was associated with an average of a 131-gram decrease in weight. Other investigators also found a decrease in birth length,¹¹ but with no decrement in ponderal index.¹² Marijuana use during pregnancy, especially in the first trimester, was associated with shortened gestation.^{13,14} An average use of marijuana ≥ 6 times per week was associated with 0.8-week reduction in length of gestation.¹³ First trimester use of marijuana also increased the odds of minor physical abnormalities in the newborn.¹⁴

Prenatal marijuana exposure has been associated with irritability, an increase in body motility, tremors, startles, poor habituation to visual stimuli, abnormal reflexes, and symptoms similar to mild withdrawal.^{15,16} These findings differed from those of Dreher et al,¹⁷ who found neonates born to marijuana users with higher socioeconomic class had no evident neurobehavioral alterations. Barros et al,¹ in this issue of *The Journal*, examined newborn infants born to adolescent mothers who used marijuana during pregnancy and compared their findings with non-exposed infants. They found alteration in neurobehavior with the Neonatal Intensive Care Unit Network Neurobehavioral Scale (NNS),¹⁸ an assessment similar to Brazelton's¹⁹ Neonatal Behavioral Assessment Scale. The NNS has been modified to assess neurobehavioral performance of high-risk infants, including those born after in utero drug exposure. Infants exposed to marijuana in utero had higher scores in arousal, lower scores in regulation, and higher scores in excitability than non-exposed infants. After in utero exposure to biological risks from marijuana, the needs of the infant with altered neurobehavior can easily add to the stresses of a substance-using adolescent parent. Furthermore, the neurobehavioral alterations, whether manifestations of withdrawal or toxic effects, may be predictors of long-term effects.²⁰

A major issue for the clinician raised by the study of Barros et al¹ is marijuana use by pregnant adolescents. In 2004, >40% of the US population older than 12 years had tried marijuana or hashish at least once, and of these, 2,236,000 were girls between 12 and 17 years old.²¹ In 2003-2004, in pregnant adolescents 15 to 17 years old, the rate of marijuana use was estimated to be 12.1%, which is not a significantly different rate of use from adolescents who were not pregnant and higher than the rate of 3.6% for all pregnant women of child bearing age, 15 to 44 years old.²¹ In the study by Barros et al,¹ 4.6% of the adolescent mothers used marijuana during pregnancy. At the same institution, Mitsuhiro et al, in a study of 1000 teen pregnant women, found a 4% rate in the use of marijuana, a 1.7% rate in the use of cocaine, and a 3% rate in the use of both marijuana and cocaine.²² Drug use in some adolescents may decline later in pregnancy, but those issues associated with adolescent pregnancy and substance use are not likely to resolve after delivery.

The psychosocial stressors encountered during adolescence may predispose girls to the early initiation of

sexual behavior and pregnancy. These stressors include household substance abuse, household mental illness, and adverse childhood events (exposure to intimate partner violence, incarcerated family member, verbal abuse, physical abuse, sexual abuse, divorced or separated parents).²³ These stressors and additional factors such as the lack of parental supervision, support, or both, poor family communication, poor academic achievement, low self-esteem, and poor mental health could predispose a girl to both drug use and adolescent pregnancy.⁹ Thus, it is no surprise that adolescent pregnancy is unintended in approximately 90% of instances.²⁴

The factors placing the adolescent at risk for drug use and unplanned pregnancy are also some of the factors that may predispose her to obstetric complications. Early sexual behavior leads to the acquisition of sexually transmitted diseases that may affect both mother and fetus. With unintended pregnancy, prenatal care may be lacking; poor nutritional status may affect fetal growth. Young teenagers weigh less, gain less weight during pregnancy, and are more likely to deliver a low birth weight or a growth restricted infant.²⁵ Jolly et al²⁶ reported increased risk of preterm labor before 32 weeks' gestation, maternal anemia, and infection. Increased risk for maternal mortality, post-partum hemorrhage, puerperal endometritis, operative vaginal delivery, caesarian section delivery, and perinatal mortality and morbidity have also been associated with adolescent pregnancy.²⁷⁻³⁰ Higher risk of maternal deaths, early neonatal deaths, and still births have been noted with the younger adolescent mothers.^{28,31} In adolescents who also use marijuana during pregnancy, younger maternal age appeared also to increase the risk of the negative effects of marijuana.¹⁴

After unplanned adolescent pregnancy, the next question is how do teen mothers fare with parenting their first-born child? Issues of parenting stress and poor mental health³² are not uncommon among adolescent mothers.^{9,32,33} Adolescent mothers who use drugs are reported to have poorer mental and physical health than adolescents who do not use drugs.⁹ These characteristics and a number of psychosocial stressors could affect maternal-infant interaction and attachment.³⁴⁻³⁷ In a study examining the trajectories and correlates of emotional distress in pregnant and nulliparous adolescents from disadvantaged communities, the teens' level of emotional distress was noted to decrease with time.³⁸ However, in pregnant teens, the decline in emotional distress occurred at a slower pace. Factors such as physical maltreatment experience and partner support influenced the trajectory of emotional distress in the pregnant adolescents. Adolescent mothers also had higher levels of parenting stress, lower maternal self-esteem, and a higher child abuse potential, which was strongly related to lack of parenting preparation.³⁹

What happens to a newborn of an adolescent who used marijuana during pregnancy? The newborn infant, who has already sustained effects from gestational drug

exposure, is likely to have exposure to multiple threats. The newborn needs attention and care-taking to alleviate the neurobehavioral alterations, to recover from any sustained medical complications if born preterm or after obstetric complications, and to continue with optimal growth and development. However, nurturing of a child's complex needs may not be optimal when an adolescent parent lacks parenting skills and is continuing to cope with psychosocial stressors and co-morbidities that led to the drug use and unplanned pregnancy. All these factors may just be too much even for a resilient child.

The American Academy of Pediatrics²⁴ continues to address the trends and issues in adolescent pregnancy. There is a need for continued and improved culturally competent prevention programs directed not only to adolescent pregnancy but also to the prevention of substance use in young people. Recently, the Committee on Adolescent Health of the American College of Obstetricians and Gynecologists⁴⁰ published a recommendation that the initial reproductive health visit be made when a girl is between 13 and 15 years of age. This first visit would steer the young adolescent to preventive services and screening for unhealthy and risky behavior, in addition to offering reassurance about normal pubertal development, maintenance of healthy eating habits, injury prevention, and safety. We must work toward childhood health education and promotion. An important measure of success is the health and well-being of the next generation.

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